

FIG. 1

ASSOCIATION STUDIES (FIRST SCREENING)

POPULATION SAMPLE SIZE	AFFECTED CASES= 112		NON AFFECTED CONTROLS=76	
	35 SPORADIC CASES +77 FAMILIAL CASES		>65 YEARS PSA<4	

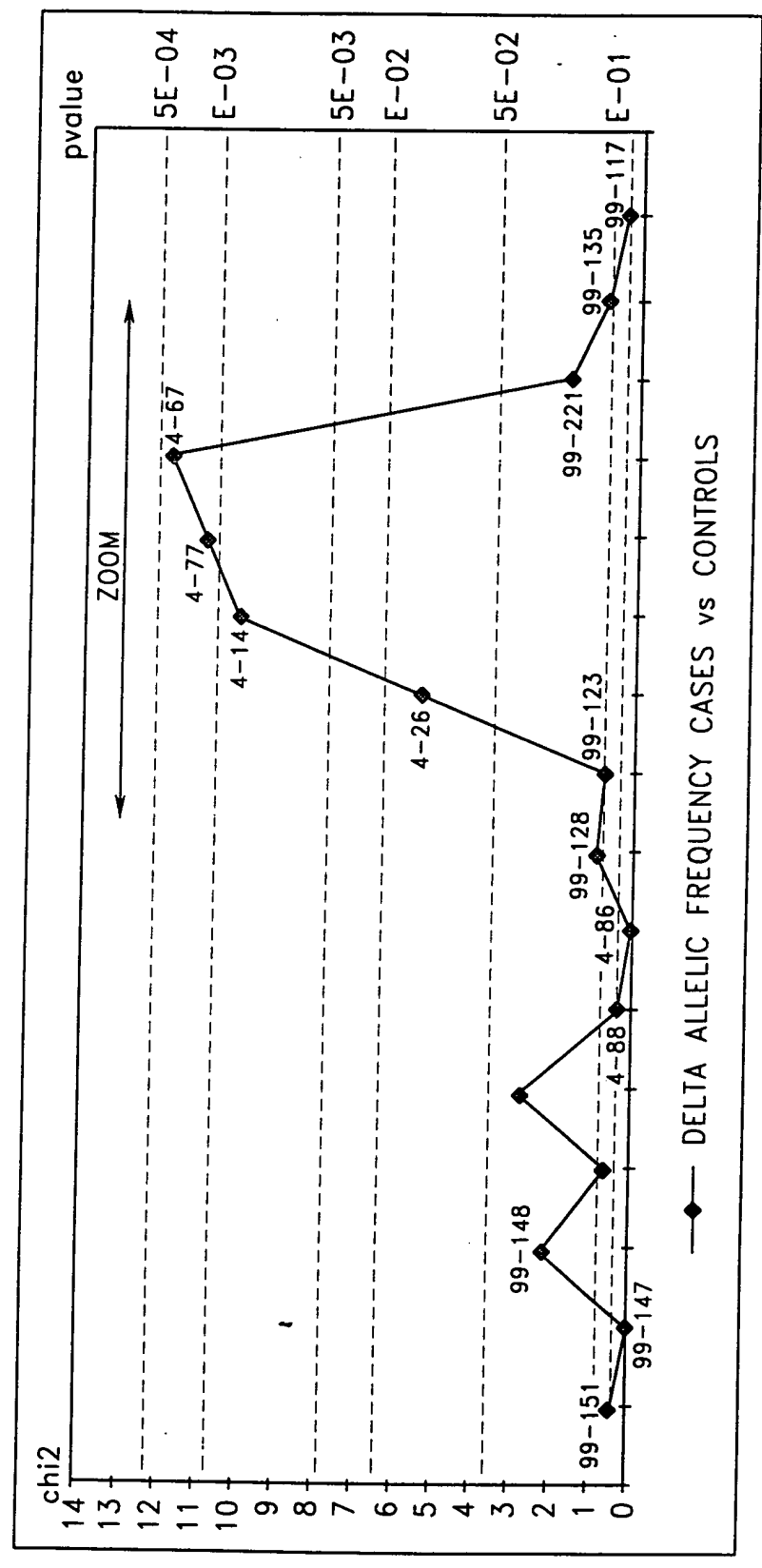


FIG.2

ASSOCIATION STUDIES (ZOOM)

CHARACTERISTICS OF POPULATIONS	AFFECTED CASES (185)	UNAFFECTED CONTROLS (104)
	47 SPORADIC CASES +138 FAMILIAL CASES	>65 YEARS PSA<4

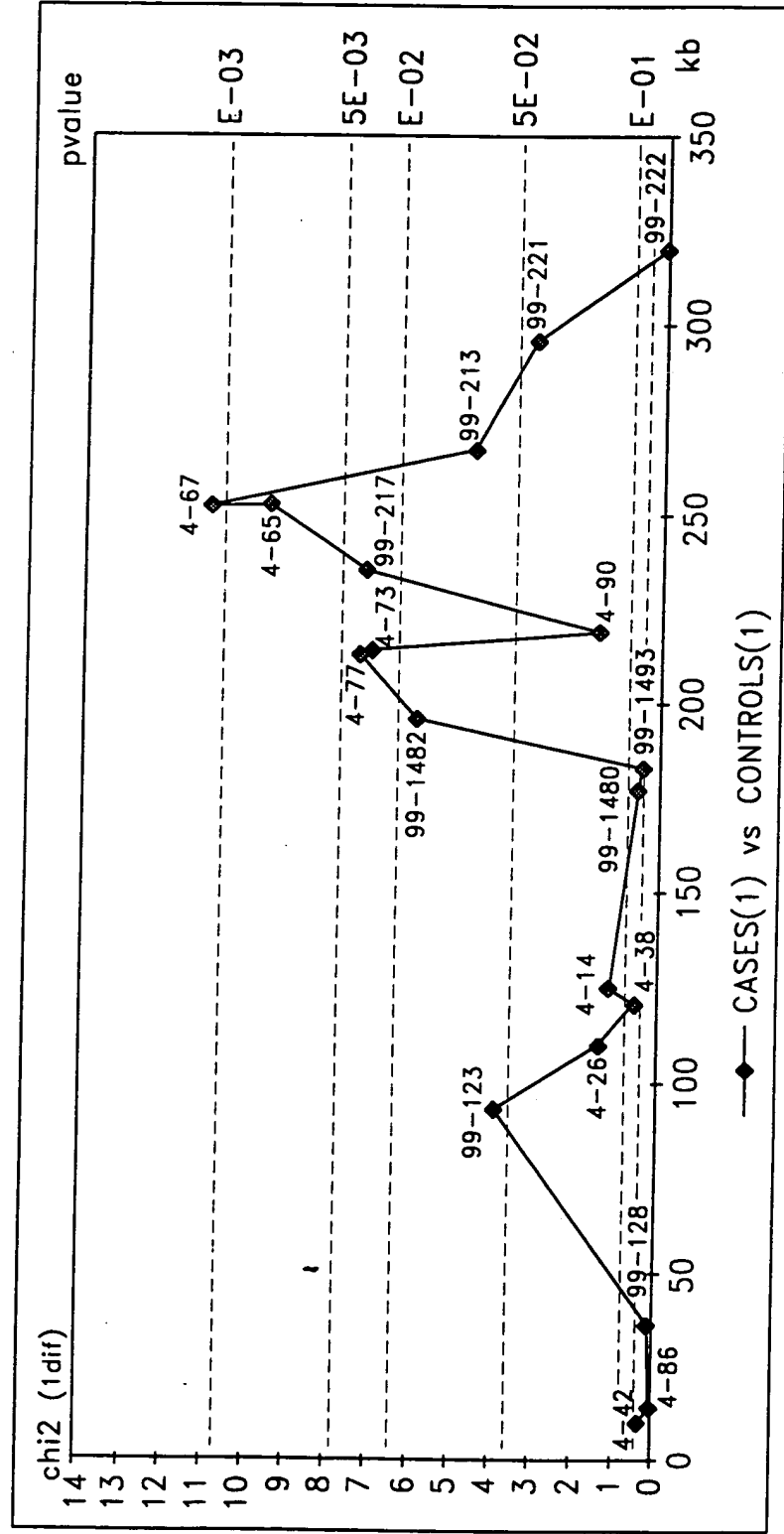
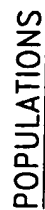


FIG.3



HAPLOTYPE SIMULATIONS (100 ITERATIONS)

MARKERS	HAPLOTYPE FREQUENCIES					RELATIV RISK	PVALUE
	C	G	T	T	A		
4-144-7799-2174-6799-21399-221	0,117	0,013	10,06	9,00E-07			

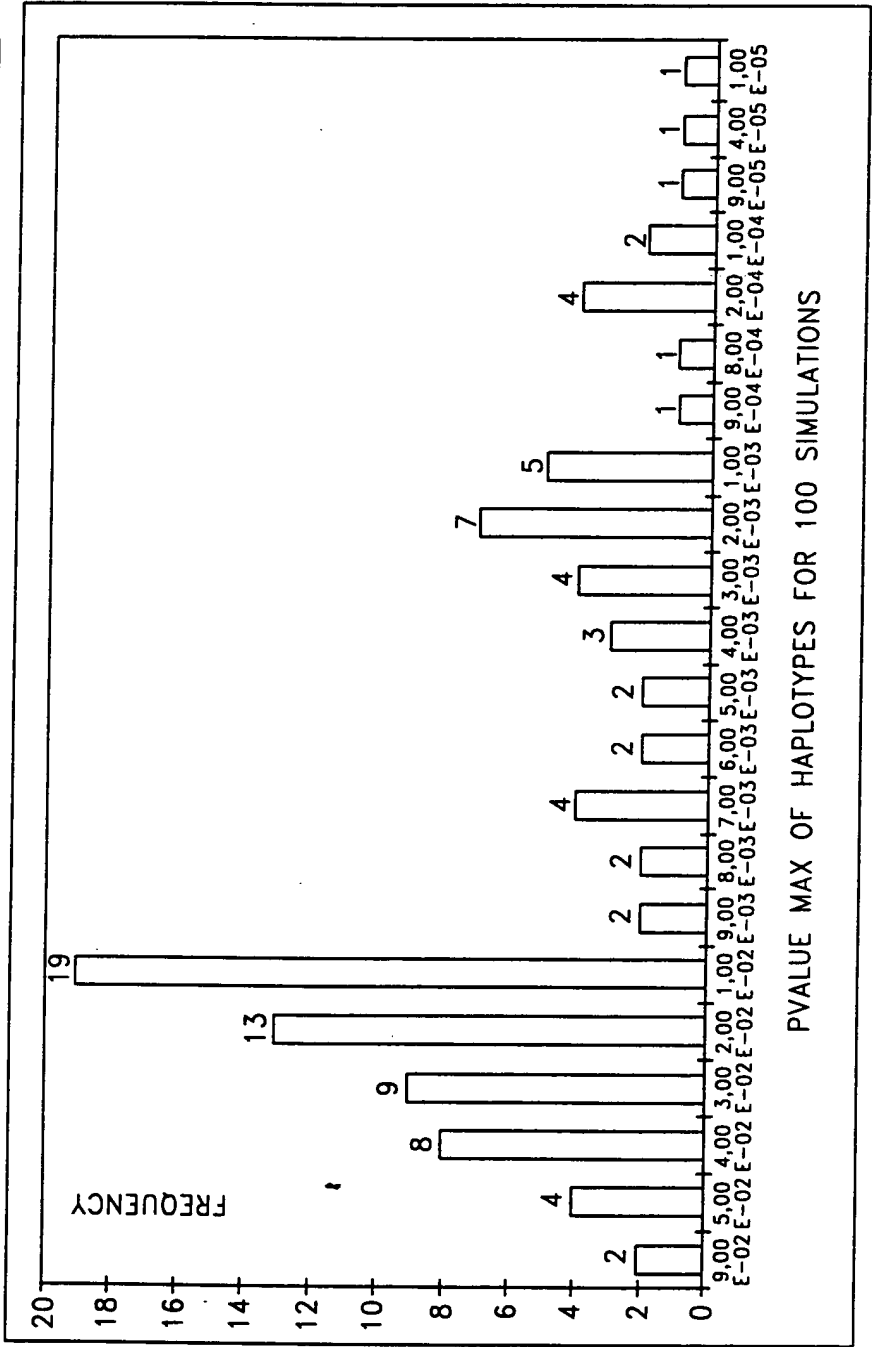


FIG.5A

BAC	MARKER	SEQ ID N°	SEQ ID N°(MUT)	PU SEQUENCE	SEQ ID N°	RP SEQUENCE	SEQ ID N°	POLYMORPHISM POSITION*	BASE	MICROSEQ. OLIGOS POSITIONS*
228	99-123	21	30	AAAGCCAGGACTAGAAGG	39	TATCAGAAAGGAGTGGG	48	24	C/T	1-23 25-47 (COMPLEMENTARY)
189	4-26	22	31	TACAGCCTGTAAAGACAC	40	TGAGGACTGCTAGGAAG	49	24	A/G	1-23 25-47 (COMPLEMENTARY)
228/189	4-14	23	32	TCTAACCTCTCATCCAAC	41	GACTGTATCCTTTGATGCAC	50	24	C/T	1-23 25-47 (COMPLEMENTARY)
189/463	4-77	24	33	TGTGATTACAGCGGCG	42	GGAAGGTACTCATCATAG	51	24	G/C	1-23 25-47 (COMPLEMENTARY)
463	99-217	25	34	GGTGGAAATTACTATATG	43	GTTTATTTTGTGTGAGCTTTG	52	24	C/T	1-23 25-47 (COMPLEMENTARY)
189/463	4-67	26	35	AAGTCCACCTTCTCAAGC	44	TGAAAGAGTTTATGCTCTGG	53	24	C/T	1-23 25-47 (COMPLEMENTARY)
463	99-213	27	36	ATACTGGGAGCGGTGCTTC	45	TTATTGCCCCACATGCTTGAG	54	24	C/T	1-23 25-47 (COMPLEMENTARY)
463	99-221	28	37	CCCTTTTCTTCACTGCTC	46	TCATTCGTCTGGCTAGGTC	55	24	A/C	1-23 25-47 (COMPLEMENTARY)
725	99-135	29	38	TGGAAGTGTATTGCCCC	47	AAACACCTCTCCATTGTGC	56	24	A/G	1-23 25-47 (COMPLEMENTARY)

FIG. 6A

*: POSITIONS ARE GIVEN RELATIVE TO THE SEQUENCE OF THE CORRESPONDING MARKER (i.e. SEQ ID N° 21-38 AND 57-62)

BAC	MARKER	SEQ ID N°	SEQ ID N°(MUT)	PU SEQUENCE	SEQ ID N°	RP SEQUENCE	SEQ ID N°	POLYMORPHISM POSITION*	BASE	MICROSEQ. OLIGOS POSITIONS*
189/463	99-1482	57	60	ATCAAATCAGTGAAGTCTGAG	63	ACAAATCTATATAAGGCTGG	66	24	A/C	1-23 25-47 (COMPLEMENTARY)
463	4-73	58	61	ATCGCTGGAACATTTCTGG	64	CTCTTGGTTAAACACGAGTG	67	24	G/C	1-23 25-47 (COMPLEMENTARY)
463	4-65	59	62	GATTAAAGCTACGCTATTAG	65	TGGCTGTGCAITTTCTCC	68	24	C/T	1-23 25-47 (COMPLEMENTARY)

FIG. 6B

*: POSITIONS ARE GIVEN RELATIVE TO THE SEQUENCE OF THE CORRESPONDING MARKER (i.e. SEQ ID N° 21-38 AND 57-62)

FIG. 7

EXON Phase	START	END	5' SPsite	PHASE	3' SPsite
Ex1 +0	2001	2216			GTGAGC
Ex2 +1	18196	18265	TAG	+0	GTTTGTA
Ex3 +0	23717	23832	CAG	+2	GTAAC
Ex4 +0	25571	25660	CAG	+0	GTAAGA
Ex5 +2	34669	34759	CAG	+0	GTAAGT
Ex6 +1	40688	40846	TAG	+1	GTAAGT
Ex7 +2	48070	48193	TAG	+2	GTGAGT
Ex8	50182	54523	TAG	+1	
ATG codon	2031	2033			
STOP codon	50405	50407			
POLY Ad site	54445	54450			

FIG. 7

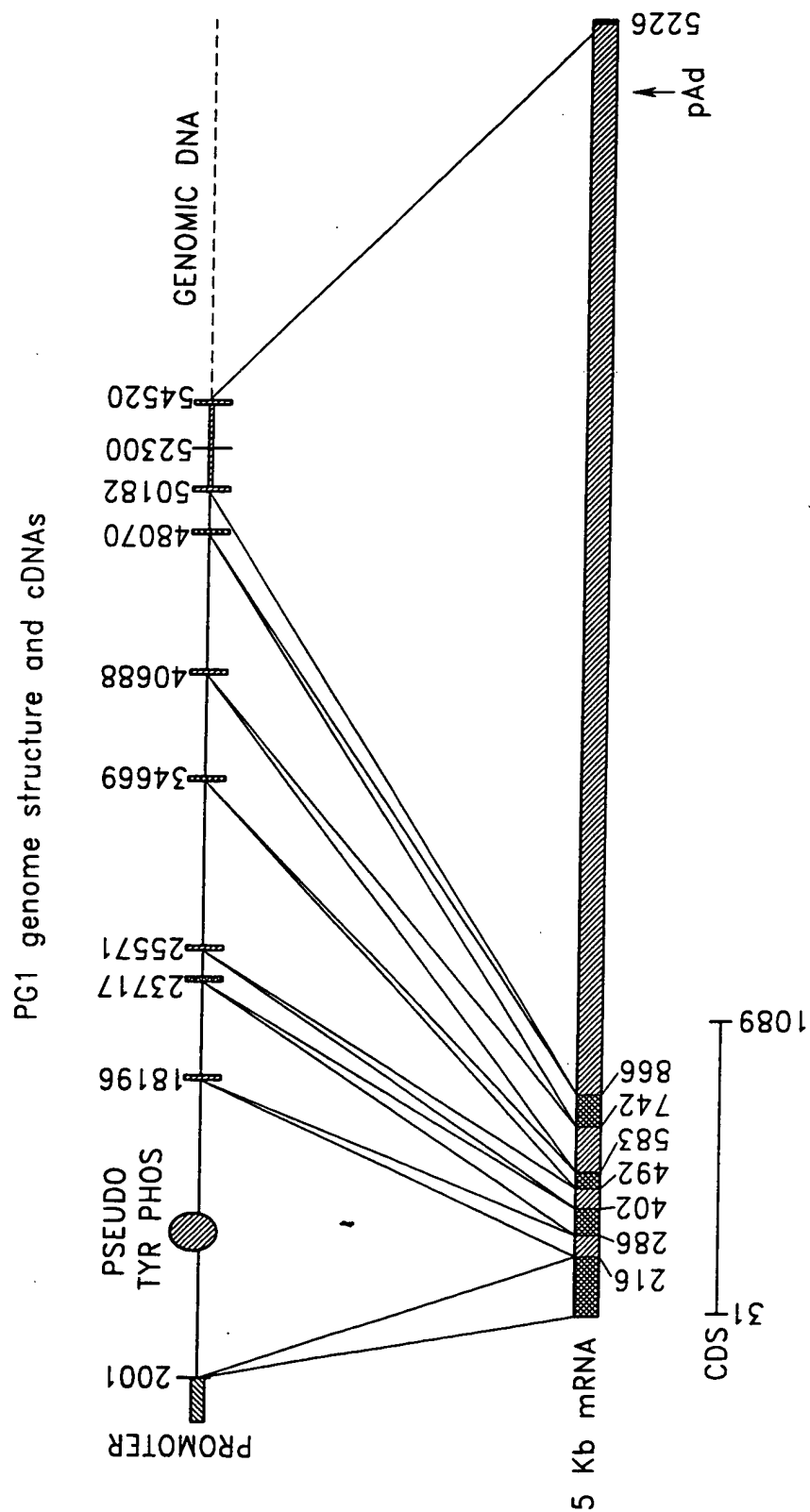
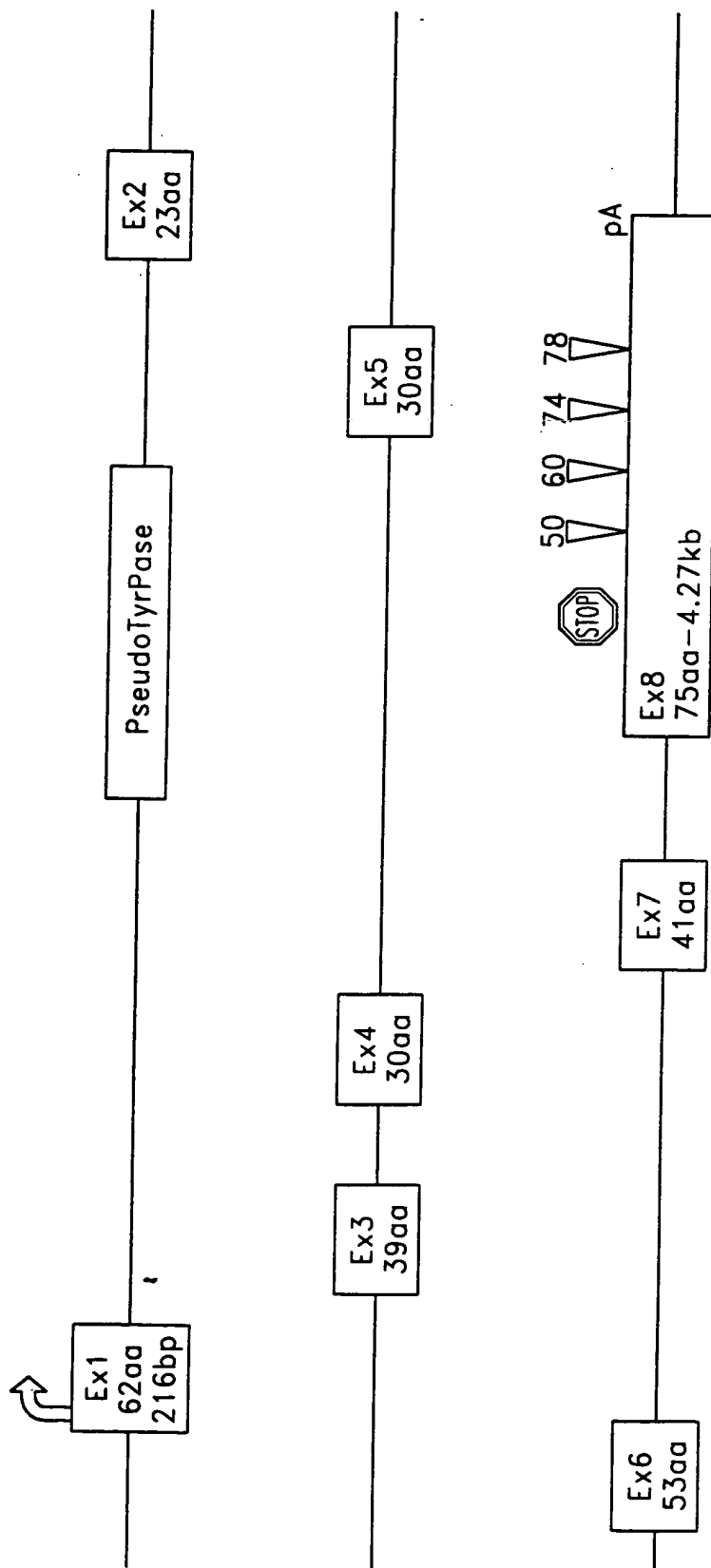


FIG.8

Prostate Gene 1

FIG. 8B



		box 1	box 2	box 3
PG1	Hs	NHQ 81-83	FPEGTR 160-165	LDAIYDVTV 211-219
AF003136 (Genbank)	Ce	NHQ 630-632	FPEGTR 712-717	LDAIYDVTV 762-770
Z72511 (Genbank)	Ce	48 NHR 50	FPEGTD 129-134	VEYIYDITI 204-212
P38226 (Swissport)	Sc	111 NHQ 113	FPEGTN 223-228	IESLYDITI 271-279
P33333 (Swissport)	Sc	81 NHQ 83	FPEGTR 154-159	-
Z49770 (Genbank)	Sc	116 NHQ 118	FPEGTN 215-220	LDAIYDVTI 265-273
P26647 (Swissport)	Ec	72 NHQ 74	FPEGTR 145-150	-
Z49860 (Genbank)	Bn	-	FVEGTR 90-95	VPAIYDMTV 138-146
U89336 (Genbank)	Hs	95 NHQ 97	FPEGTR 168-173	-
U56417 (Genbank)	Hs	103 NHQ 105	FPEGTR 176-181	-
AB005623 (Genbank)	Mm	100 NHQ 102	FPEGTR 173-178	
Z29518 (Genbank)	Zm	91 NHR 93	FVEGTR 170-175	VPAIYDTTV 218-226

Hs = Homo sapiens, Ce = Caenorabibitis elegans, Ec = Escherichia coli;
 Sc = Saccharomyces cerevisiae, Bn = Brassica napus, Zm = Zea maize,
 Mm = Mus Musculus

- = pattern absent from protein sequence

Note: Functional acyl glycerol transferases all contain boxes 1 and 2 and not box 3. Proteins most related to PG1 contain the 3 boxes with a high degree of conservation.

FIG. 9

TOP SECRET

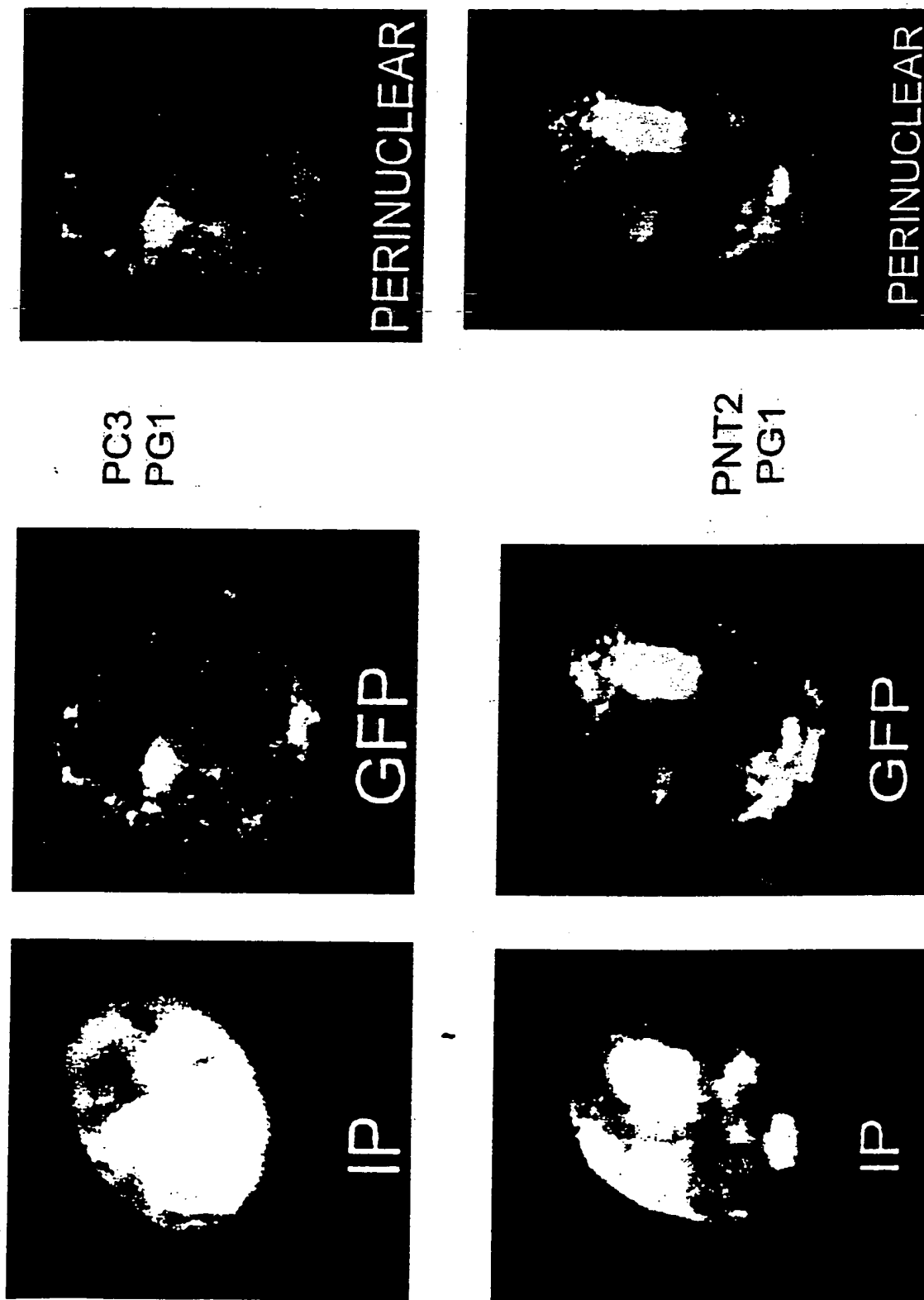


FIG. 10

TOP SECRET

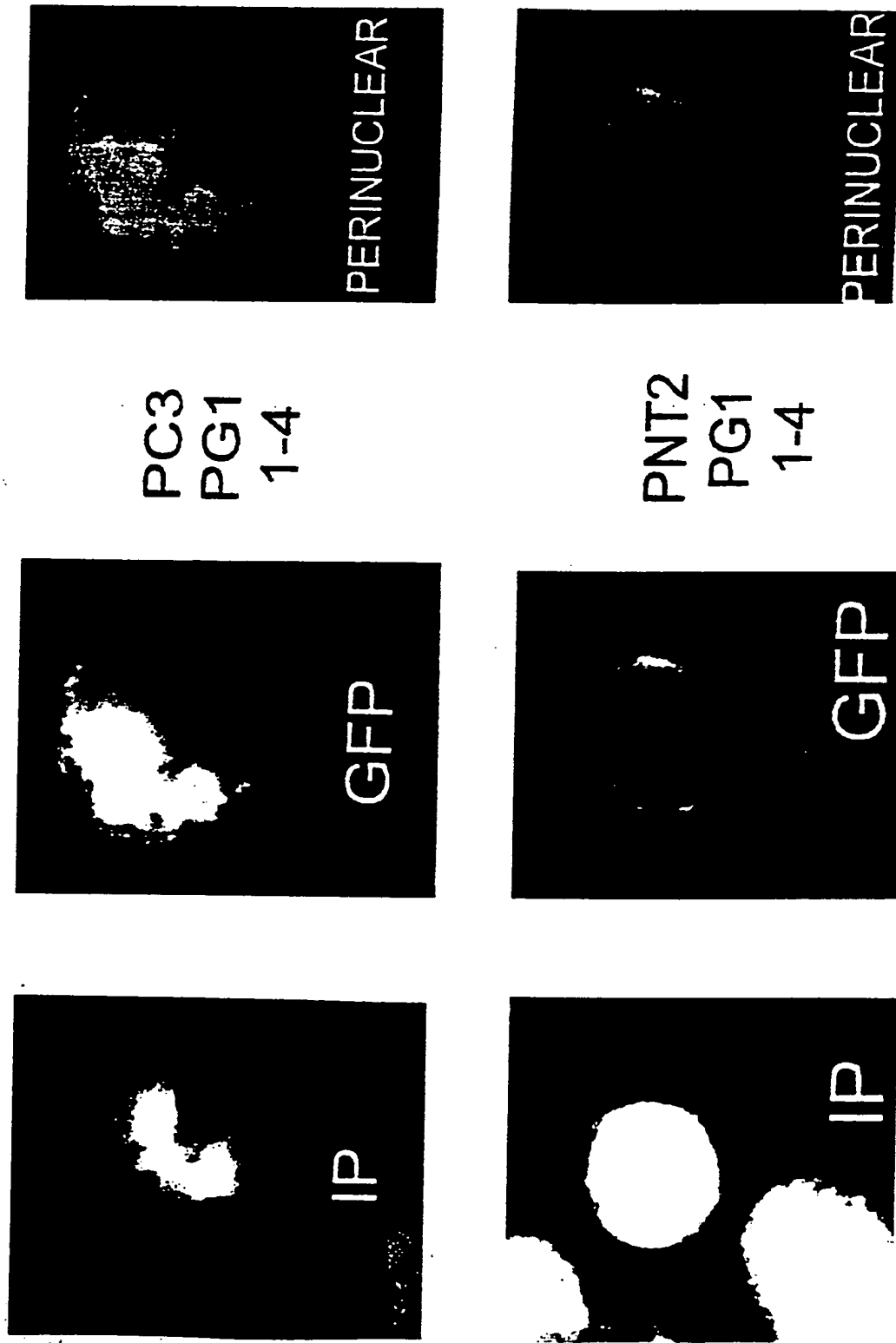
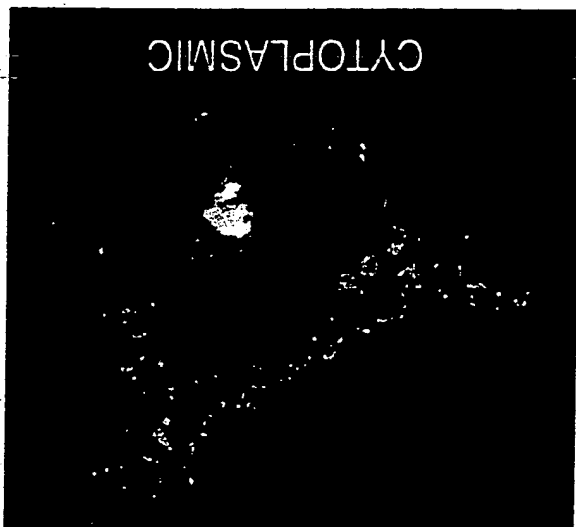
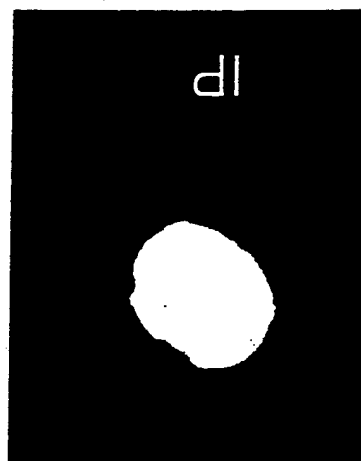
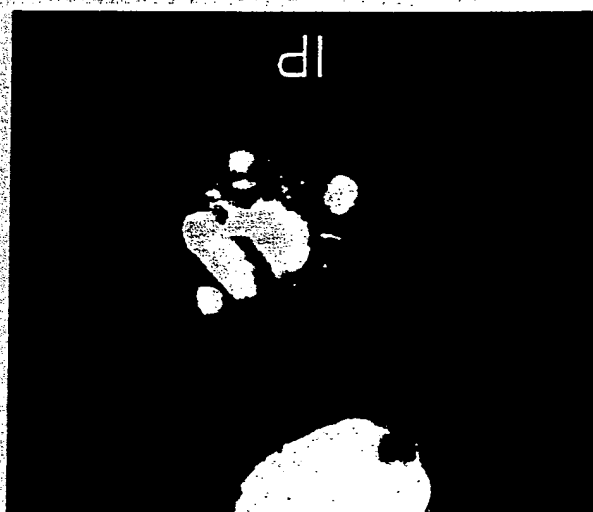


FIG. 11



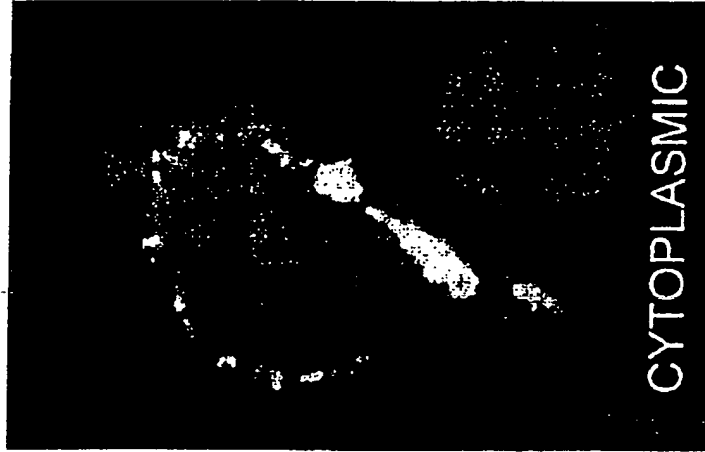
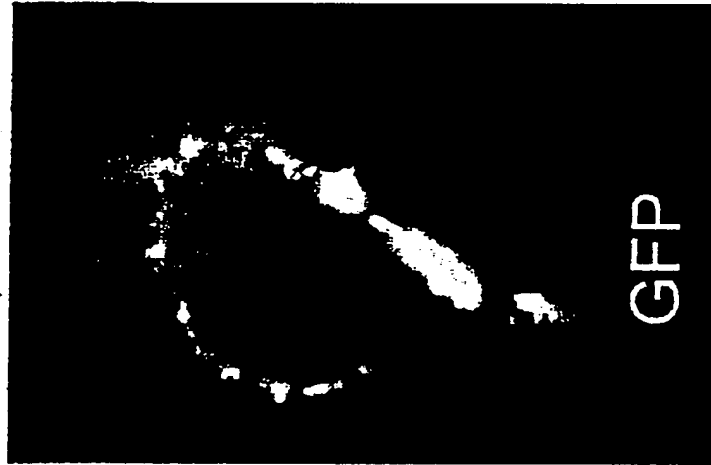
PNT2 PG1 1-5



PC3
PG1
1-5

[illegible]

TOPP 3632560



PNT2 PG1 mut229

FIG. 13

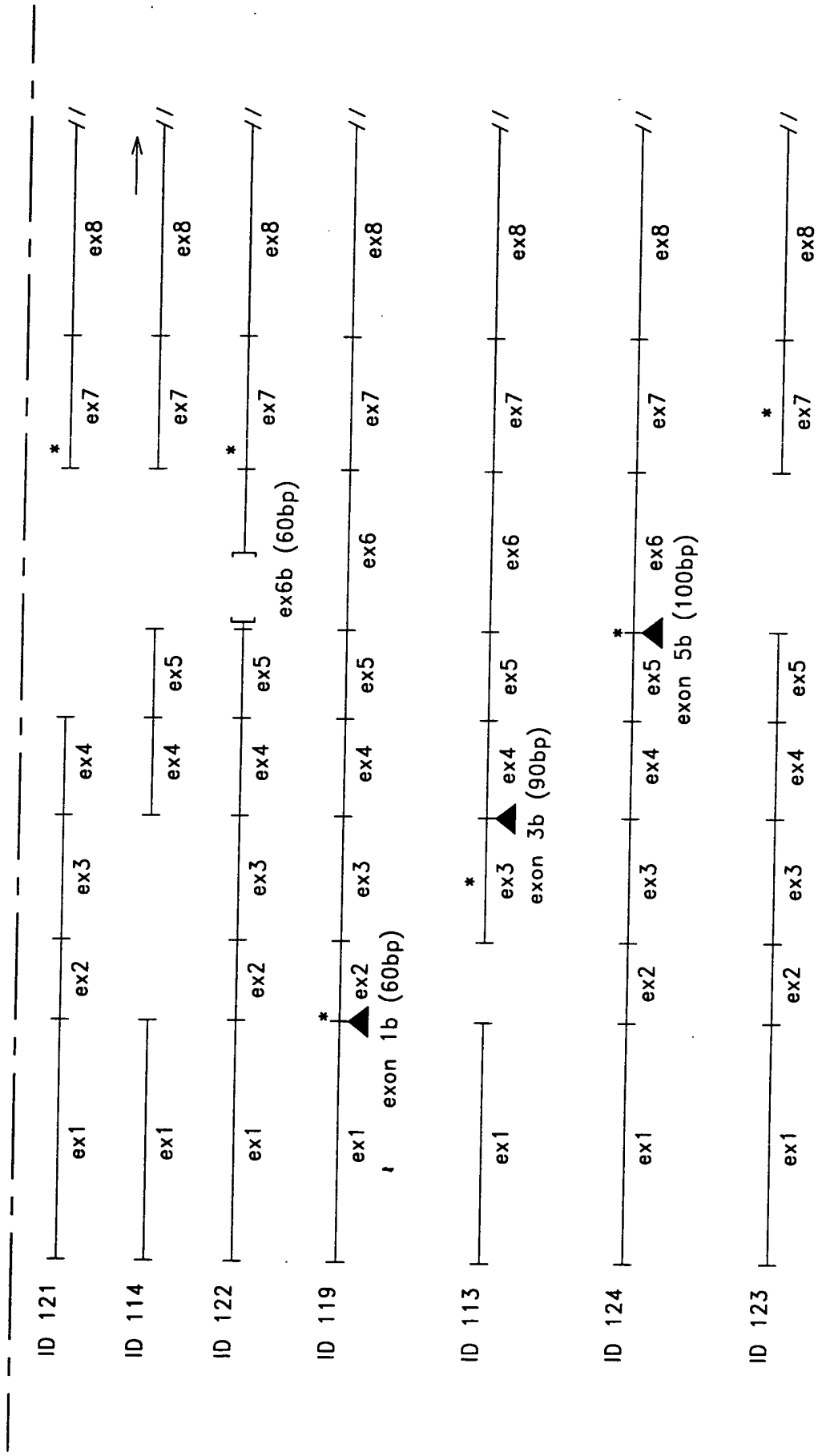


FIG. 14B

Combination of exons of PG1 gene discovered
by PCR with primers specific for exon borders

Printer	Clones	prostate	PNT1A	PNT1B	PNT2	LnCaPFCG	LNCaPJMB	CoHPV	Du145	PC3	ECP5	ECP6	ECP7	ECP8	ECP9	ECP10	ECP11	ECP12	ECP13	ECP14	ECP15	ECP16	ECP17	ECP18	ECP19	ECP20	ECP21	ECP22	ECP23	ECP24
PG1exon13	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PG1exon14	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PG1exon15	+	-	-	-	-	-	-	NT	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
PG1exon16	-	+	-	+	+	-	-	NT	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-
PG1exon17	+	+	+	+	+	+	+	NT	+	+	-	-	+	-	-	-	+	+	+	+	+	+	+	+	-	-	+	+	-	+
PG1exon18	+	+	+	+	+	-	-	NT	+	+	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-
PG1exon24	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PG1exon25	+	+	-	+	+	-	-	NT	+	-	-	-	-	-	-	-	+	-	-	-	+	-	-	-	-	-	-	-	+	+
PG1exon26	+	+	+	+	+	+	+	NT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PG1exon27	-	-	-	+	+	-	-	NT	+	-	-	-	-	-	-	-	-	+	-	-	+	-	-	-	-	-	-	-	+	+
PG1exon28	-	-	+	-	-	-	-	NT	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
PG1exon35	-	+	+	+	+	+	+	NT	+	+	-	-	-	-	-	-	+	+	-	+	+	+	-	-	+	+	+	+	-	-
PG1exon36	+	+	+	+	+	+	+	NT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PG1exon37	-	-	-	-	-	-	-	NT	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
PG1exon38	-	-	-	-	-	-	-	NT	-	+	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	+	-	-	-
PG1exon46	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PG1exon47	+	+	+	+	+	+	+	NT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PG1exon48	-	-	-	-	+	-	-	NT	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
PG1exon57	+	+	+	+	+	+	+	NT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PG1exon58	-	-	-	-	-	+	+	NT	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-
PG1exon68	-	+	+	-	+	+	+	NT	+	+	-	-	-	-	+	+	-	+	+	-	+	-	-	+	-	-	+	-	+	+
PG1exon11b	+	+	+	+	+	+	+	NT	+	+	-	+	-	+	+	+	+	+	+	+	-	-	+	-	-	+	+	+	-	+
PG1exon1b2	+	+	+	+	+	+	+	NT	+	+	-	+	-	+	+	+	+	+	+	+	-	+	-	-	+	+	+	-	+	
PG1exon1b3	+	+	+	+	+	+	+	NT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PG1exon1b4	+	-	+	+	+	+	+	+	+	+	-	-	+	-	+	+	-	-	-	+	+	+	+	-	+	+	-	+	-	
PG1exon1b5	+	-	+	+	+	+	+	NT	+	+	-	-	+	-	-	+	+	-	-	+	+	+	-	+	+	-	+	+	+	-
PG1exon1b6	+	+	+	+	+	+	+	NT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PG1exon1b7	+	-	+	+	+	+	+	NT	+	+	+	+	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-
PG1exon1b8	-	-	+	-	+	-	-	NT	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
PG1exon3b4	+	+	+	+	+	+	+	NT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PG1exon3b5	-	-	+	+	-	-	-	NT	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
PG1exon3b6	+	+	+	+	+	+	+	NT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PG1exon3b7	+	-	+	+	-	+	+	NT	-	+	-	+	-	-	-	-	-	-	-	-	+	+	-	-	+	-	-	-	-	-
PG1exon3b8	-	-	-	-	-	-	-	NT	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
PG1exon5b6	+	+	-	-	-	-	+	NT	-	+	-	+	-	-	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-
PG1exon5b7	+	-	+	+	+	+	+	NT	+	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-
PG1exon5b8	-	-	-	+	-	-	-	NT	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
PG1exon56b	+	+	+	+	+	+	+	NT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PG1exon46b	+	+	+	+	+	+	+	NT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PG1exon36b	+	+	+	+	+	+	+	NT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PG1exon26b	+	+	+	+	+	+	+	NT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PG1exon16b	+	+	+	+	+	+	+	NT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

[+] alternative splicing form with combination of exons 13478 instead of 1345678

FIG. 15

FIG. 16 **ASSOCIATION STUDIES**
HAPLOTYPE FREQUENCY ANALYSIS (chrom 8p23)

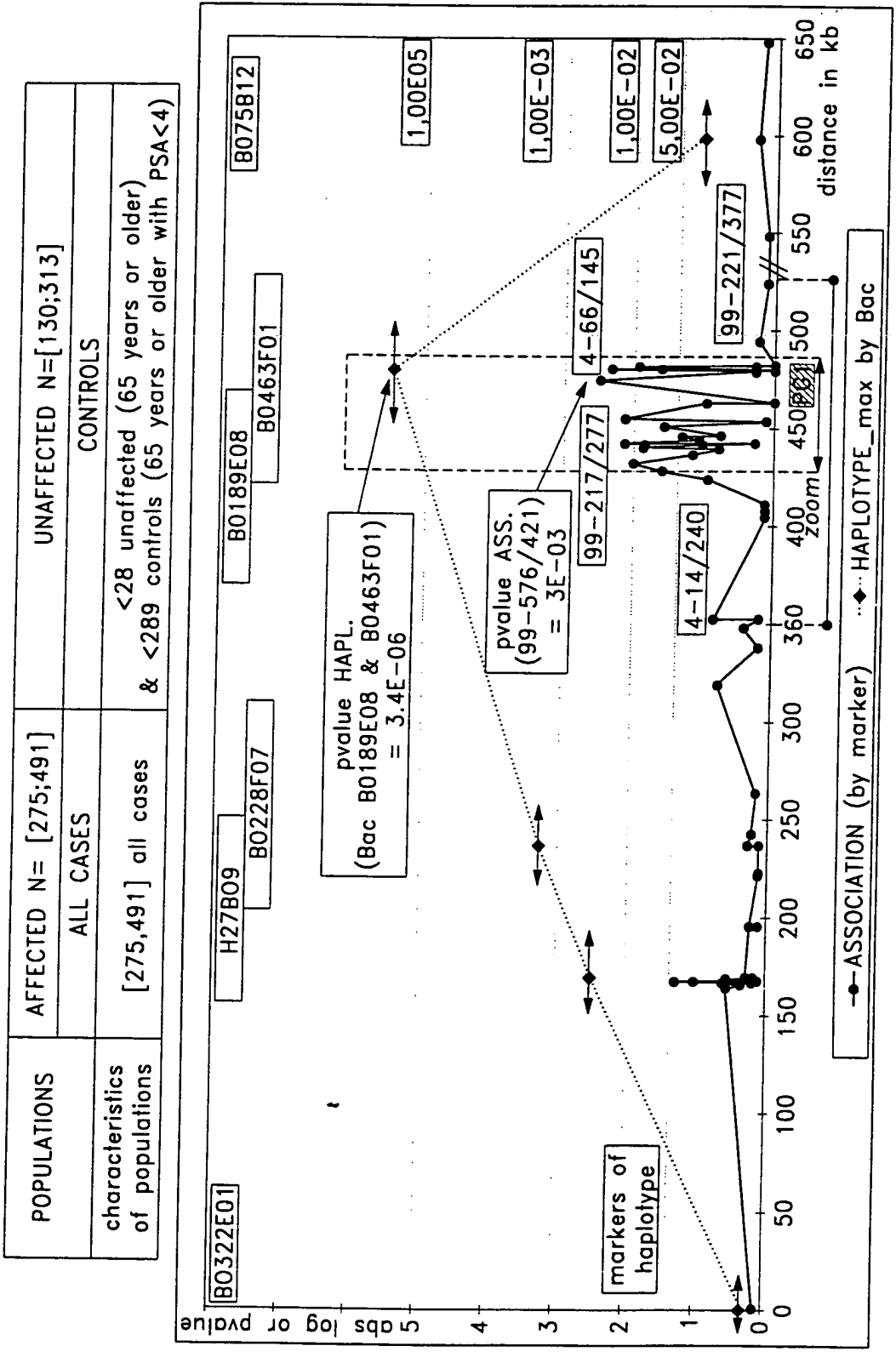


FIG. 17

ASSOCIATION STUDIES PG1 (8p23)

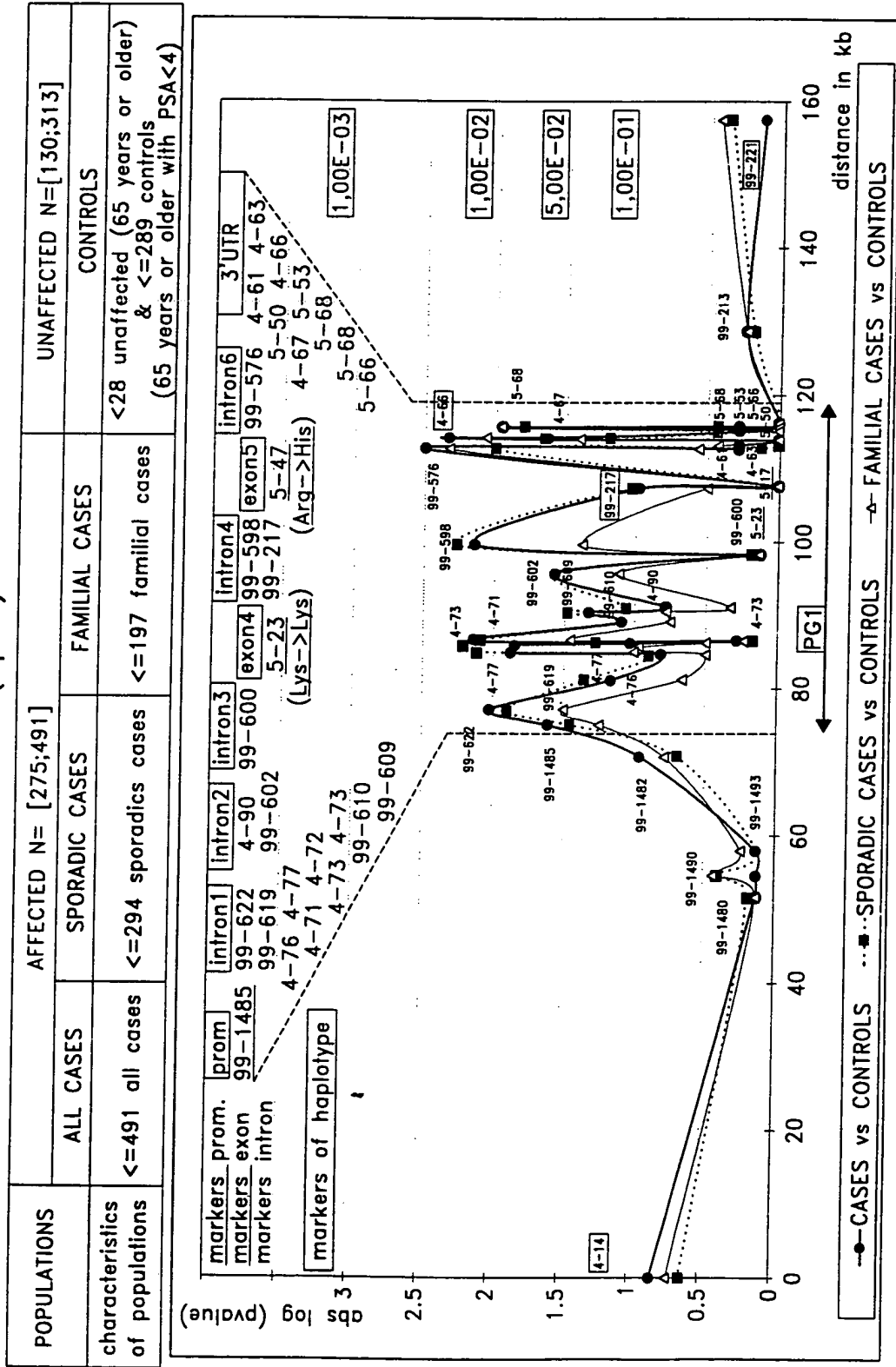
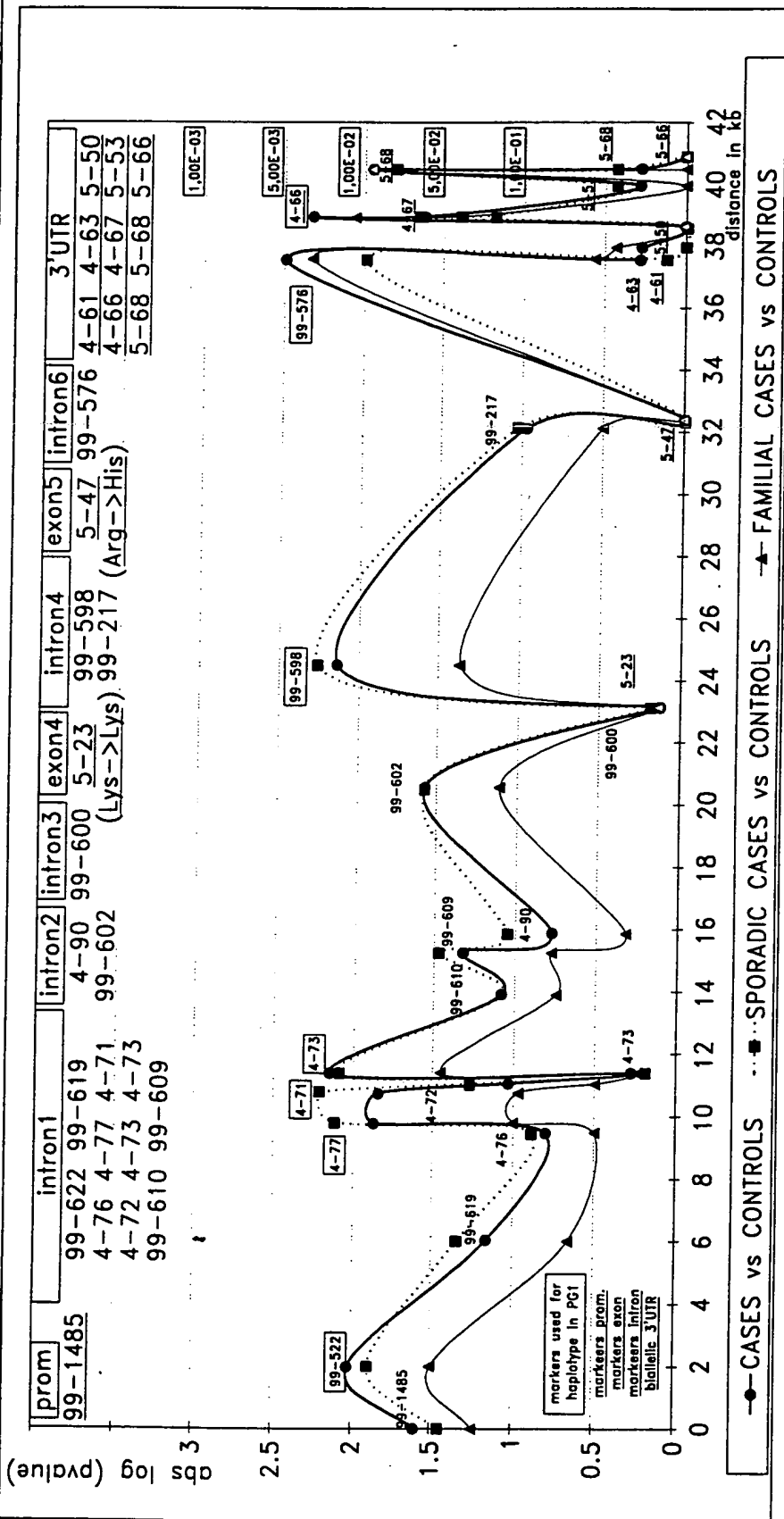


FIG. 18A

PG1 (8p23)

POPULATIONS	AFFECTED N= [275;491]			UNAFFECTED N=[130;313]	
	ALL CASES	SPORADIC CASES	FAMILIAL CASES	CONTROLS	
characteristics of populations	<=491 all cases	<=294 sporadics cases	<=197 familial cases	<28 unaffected (65 years or older) & <=289 controls (65 years or older with PSA<4)	



name of markers	PG1	Polym.	Freq(cas)	Freq(controls)	abs diff % (fq(cases)- fq(controls))	Odd Ratio	Pvalue	Freq(randoms)	Attributable Risk
99-1485/251	prom	G*/T	0.32	0.24	7.4	1.44	2.53E-02	0.29	17.58
99-622/95	in1	G/T	0.52	0.42	10.1	1.51	9.64E-03	ND§	ND
99-619/141	in1	C/T	0.28	0.22	5.8	1.37	6.93E-02	ND	ND
4-76/222	in1	G/A	0.43	0.38	5	1.23	1.57E-01	0.41	13.15
4-77/151	in1	G/C	0.34	0.26	7.4	1.43	1.35E-02	0.31	18.16
4-71/233	in1	A/G	0.34	0.26	8.3	1.49	1.43E-02	0.28	18.64
4-72/127	in1	A/G	0.36	0.30	5.7	1.29	9.43E-02	0.31	13.25
4-73/134	in1	G/C	0.52	0.42	9.7	1.48	7.29E-03	0.52	26.76
99-610/250	in1	G/A	0.43	0.37	6.2	1.30	8.33E-02	ND	ND
99-609/225	in1	A/T	0.37	0.30	7	1.36	4.83E-02	ND	ND
4-90/283	in2	A/C	0.29	0.25	4.4	1.25	1.68E-01	0.28	9.32
99-602/258	in2	A/G	0.33	0.25	7.4	1.44	2.69E-02	ND	ND
99-600/492	in3	T/A	0.34	0.34	0.3	1.01	7.52E-01	ND	ND
99-598/130	in4	G/A	0.35	0.25	9.2	1.55	7.29E-03	ND	ND
99-217/277	in4	T/C	0.31	0.28	3.8	1.20	1.07E-01	0.28	8.46
99-576/421	in6	G/C	0.27	0.17	9.2	1.72	3.18E-03	0.24	18.40
4-61/269	3'UTR	G/A	0.01	0.00	0.3	1.76	0.527§	ND	ND
4-66/145	3'UTR	C/T	0.25	0.19	6.2	1.43	4.68E-03	0.24	13.16
4-67/40	3'UTR	T/C	0.25	0.20	4.9	1.33	2.39E-02	0.24	10.97

§ Test Fisher-§ ND: Not done -* disease associated allele / not associated allele

FIG. 18B

HAPLOTYPE FREQUENCY ANALYSIS

POPULATIONS	AFFECTED	UNAFFECTED
sample sizes	CASES (n=491)	CONTROLS (n=317)
characteristics of populations	294 sporadic cases + 197 familial cases	28 unaffected (65 years or older) + 289 controls (65 years or older with PSA<4)

PG1 (8p23)			4-14/240	99-217/277	4-66/145	99-221/377
distance between mks						
size (cases vs controls)						
frequency % (cases/controls)						
abs diff freq. all.(cases-controls)						
pvalue						
Hardy Weinberg Disequilibrium		cases				
		controls				
HAP 1 <43kb>	PT2	451 vs 297				
HAP 2 <17kb>		451 vs 296				
HAP 3 <117kb>		452 vs 299				
HAP 4 <100kb>		479 vs 302				
HAP 5 <60kb>		476 vs 300				
HAP 6 <160kb>		476 vs 303				
HAP 7 <160kb>	PT3	447 vs 297				
HAP 8 <60kb>		446 vs 294				
HAP 9 <117kb>		450 vs 296				
HAP 10 <160kb>		474 vs 300				
HAP 11 <160kb>		445 vs 294				
			<100kb>	<17kb>	<43kb>	
			481vs305	481vs302	481vs300	481vs 303
			65,7/62,1(C)	31,3/27,5(C)	25,1/19(C)	42,7/42,91 (A)
			3.6	3.8	6.2	0
			1.47E-01	1.07E-01	4.68E-03	7.52E-01
			5.84E-01	6.55E-01	2.54E-01	5.84E-01
			4.80E-01	2.21E-01	3.71E-01	2.54E-01
			C A			
			T C			
			C C			
			T A			
			C C			
			C A			
			T C A			
			C C A			
			T T A			
			C T A			

haplotype frequencies		Odd ratio	Chi-S	Pvalue	
cases	controls				
0.116	0.067	1.83	9.85	(1.7e-03)	***
0.243	0.183	1.43	7.49	(6.2e-03)	**
0.182	0.130	1.49	7.18	(7.3e-03)	**
0.217	0.188	1.20	1.88	(1.7e-01)	*
0.155	0.132	1.20	1.54	(2.1e-01)	*
0.373	0.346	1.12	1.16	(2.7e-01)	*
0.095	0.042	2.39	14.62	(1.3e-04)	*****
0.117	0.065	1.93	11.33	(7.3e-04)	***
0.178	0.125	1.53	7.80	(5.2e-03)	**
0.114	0.089	1.32	2.44	(1.1e-01)	*
0.095	0.032	3.18	21.59	(3.4e-06)	*****

FIG. 19B HAPLOTYPE FREQUENCY ANALYSIS PG1 (8p23)

markers of haplotype Max	4-14/240	99-217/277 in4	4-66/145 3'UTR	99-221/377	
	C	T	C	A	
distance between mks	<100kb>		<17kb>		<43kb>

PG1	sample sizes	haplotype frequencies		odd ratio	chl-S	P value
		cases vs control	cases	controls		
cases vs control	455 vs 294	0.095	0.032	3.18	21.59	3.40E-06 *****
cases (<=65 years) vs controls	171 vs 294	0.105	0.032	3.56	20.91	4.60E-06 *****
cases (>65 years) vs control	271 vs 294	0.079	0.032	2.60	12.13	4.80E-04 ****
sporadic cases vs controls	266 vs 294	0.096	0.032	3.23	19.73	8.60E-06 *****
sporadic cases (<=65 years) vs controls	85 vs 294	0.095	0.032	3.20	12.04	5.00E-04 ****
sporadic cases (>65 years) vs controls	178 vs 294	0.085	0.032	2.82	12.75	3.50E-04 ****
informative sporadic cases vs controls	67 vs 294	0.062	0.032	2.00	2.70	9.40E-02 **
familial cases vs controls	179 vs 294	0.098	0.032	3.32	18.33	1.80E-05 *****
familial cases (<=65 years) vs controls	86 vs 294	0.112	0.032	3.83	17.98	2.20E-05 *****
familial cases (>65 years) vs controls	93 vs 294	0.075	0.032	2.48	6.59	1.00E-02 **
familial cases (>=3 caP) vs controls	79 vs 294	0.123	0.032	4.26	21.33	3.70E-06 *****

HAPLOTYPE FREQUENCY ANALYSIS (PG1)

ND: Not Done

Comparison of Pvalue between nb of mks for haplotype
(19 mks of PG1)

FIG. 21

GENE	# of markers	# of 2 mks combinations	# of 3 mks combinations	# of mks combinations
PG1	19	171	969	3876

CUMULATIVE FREQUENCY HISTOGRAM OF Chi-square statistics (Chi-S) for PG1

